

Francis H. Case

Department of Chemistry, Temple University, Philadelphia, PA 19122

and

A. A. Schilt

Department of Chemistry, Northern Illinois University, DeKalb, IL 60115

Received March 23, 1979

Certain oximes were prepared from 2-quinolylmethyl 2-pyridinyl ketone and 2-(1,10-phenanthrolyl)methyl 2-pyridinyl ketone. Also, the preparation of two series of hydrazones was effected: one from 2-acetylquinoline and one from 2-acetyl-1,10-phenanthroline. The latter compound and 2-(2-quinolyl)-1,10-phenanthroline were also synthesized. All the compounds were tested for their metal-chelation properties.

J. Heterocyclic Chem., 16, 1135 (1979).

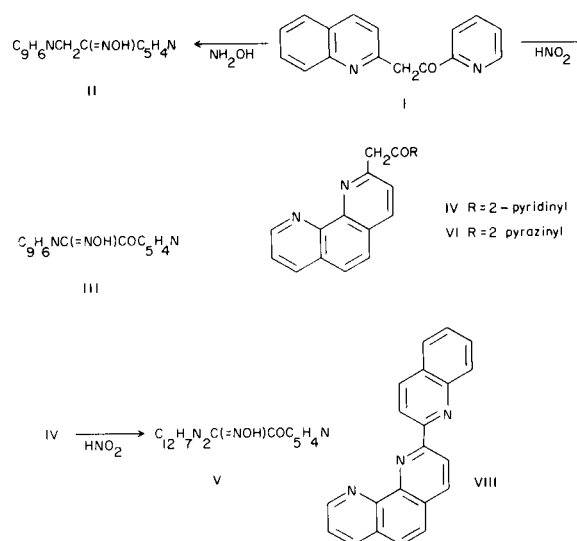
In previous communications we have described the preparation and chelation properties of oximes of pyridinyl and diazinylmethyl ketones (1), and also of certain pyrimidinyl and diazinyll hydrazones (2), containing one or more ferriin groups. We have now extended both of these researches by preparing similar derivatives of 1,10-phenanthroline and quinoline.

2-Quinolylmethyl 2-pyridinyl ketone (I) was previously prepared from the lithium derivative of quinaldine (3). We have prepared it by the action of ethyl picolinate on the sodium derivative of quinaldine in liquid ammonia, using a modification of the method employed by Behun and Levine (4) for similar ketones. The two oximes of this ketone (II,III) were then made by the action of hydroxylamine and of nitrous acid.

2-(1,10-Phenanthrolyl)methyl 2-pyridinyl ketone (IV) was synthesized from 2-methyl-1,10-phenanthroline (5) and ethyl picolinate in presence of potassium ethoxide by a method previously described (1). From IV, an oxime (V) resulted on treatment with nitrous acid, but not with hydroxylamine. 2-(1,10-Phenanthrolyl)methyl 2-pyrazinyl ketone (VI), obtained from 2-methyl-1,10-phenanthroline and methyl pyrazinoate by a similar method, yielded no oxime with either reagent.

Another part of the work involved the preparation of various hydrazones of 2-acetylquinoline, and 2-acetyl-1,10-phenanthroline. The former was prepared by the method of Campbell, *et al* (6), and the latter (VII) (hitherto unknown) was prepared by a similar method. These compounds were converted to the following hydrazones: phenyl, 2-pyridinyl, pyrazinyl, 2-pyrimidinyl and 2-thiazolyl. By the action of *o*-aminobenzaldehyde, 2-acetyl-1,10-phenanthroline was converted to 2-(2-quinolyl)-1,10-phenanthroline (VIII).

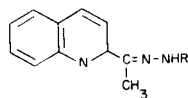
To identify compounds with promising chromogenic



properties, their reactions with the ions of iron, copper, cobalt, and nickel were investigated as a function of pH. Color formation commonly occurred over the pH range 3-11, with maximum development between pH 5 and 8. Dilution with ethanol (up to 60% by volume) was necessary to avoid precipitation problems. As expected from previous studies (8), compounds with bulky noncoordinating substituents adjacent to the ferriin reacting group failed to give colored products with iron(II), cobalt(II), or nickel(II). These include compounds III, IV, VI, VII and IX.

Results of the mole ratio determinations indicate that the substituted hydrazones of 2-acetylquinoline (X, XI, XII, and XIII) react as terdentate ligands with iron(II) to form strong chelates with ligand to metal ratios of 2:1. Thus, all four compounds exist predominantly in the *anti*-isomer form (RHN-moeity *trans* to the quinoline group), since the *syn*-isomer is capable of bidentate but

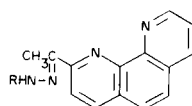
Table I
Substituted Hydrazones of 2-Acetylquinoline



Compound No.	R	M.p. (°C)	Crystallization Solvent	Formula	Analyses					
					C	Calcd. H	N	C	Found H	N
IX	Phenyl (a)	154								
X	2-Pyridinyl	161	Methanol	C ₁₆ H ₁₄ N ₄	73.26	5.38	21.36	73.25	5.45	21.26
XI	Pyrazinyl	212	Ethanol	C ₁₅ H ₃ N ₅	68.43	4.98	26.60	68.52	4.84	26.76
XII	2-Pyrimidinyl	196	Ethanol	C ₁₅ H ₁₃ N ₅	68.43	4.98	26.60	68.12	4.89	26.78
XIII	2-Thiazolyl	214	Ethanol	C ₁₄ H ₁₂ N ₄ S	62.68	4.51	20.88	62.54	4.48	20.90

(a) See Ref. 6.

Table II
Substituted Hydrazones of 2-Acetyl-1,10-phenanthroline



Compound No.	R	M.p. (°C)	Crystallization Solvent	Formula	Analyses					
					C	Calcd. H	N	C	Found H	N
			Methyl							
XIV	Phenyl	235	Cellosolve	C ₂₀ H ₁₆ N ₄	76.90	5.16	17.94	77.15	5.05	17.95
XV	2-Pyridinyl	212	Benzene	C ₁₉ H ₁₅ N ₅	72.83	4.82	22.35	72.97	4.84	22.14
XVI	Pyrazinyl	231	Ethanol	C ₁₈ H ₁₄ N ₆	68.78	4.49	26.73	68.62	4.45	26.75
XVII	2-Pyrimidinyl	241	Aqueous Ethanol	C ₁₈ H ₁₄ N ₆	68.78	4.49	26.73	68.33	4.44	26.60
XVIII	2-Thiazolyl	254	Ethanol	C ₁₇ H ₁₃ N ₅ S	63.94	4.10	21.93	63.66	4.21	21.74

not terdentate chelation.

Structural considerations indicate that the *anti*-isomers of the substituted hydrazones of 2-acetyl-1,10-phenanthroline should be capable with some difficulty of bi-, ter-, and quadridentate coordination, while the *syn*-isomers should chelate without appreciable steric difficulty only in a bidentate mode. Results of the mole ratio study reveal that these hydrazones form weak iron(II) chelates with ligand to iron ratios of 3 to 1. Hence, the ligands are bound in the bidentate mode, and it is not possible to distinguish between the two isomer possibilities on the basis of ligand to metal ratios. The instability of their iron(II) chelates is further evidenced by the observation that addition of hydroxylamine converted them to intense violet *bis*-chelates (L:M = 2:1), presumably due to conversion of the hydrazones to oximes. The biquinoline analogs did not show similar behavior.

As expected, II, with a single unhindered ferriin group, formed an iron(II) complex with a ligand to metal ratio of 3:1. Also consistent with their structures and possible terdentate action, compounds VIII and V formed strong *bis*-chelates with ligand to iron ratios closely approximating 2:1.

Limited solubility of the compounds restricts their application to solutions which contain appreciable proportions of ethanol, dimethylformamide, or other water-miscible solvent. Their chromogenic properties are interesting but not outstanding in comparison to those of many previously studied ferriin-type hydrazones (2,9). Of those described here, the most sensitive chromogenic reagents for iron, copper, cobalt, and nickel are the hydrazones of 2-acetylquinoline. These merit further attention for their potentially useful analytical applications in trace metal determinations.

Table III
Properties of Iron(II) Chelates

Ligand	Color	λ max (nm)	ϵ (l. mole ⁻¹ cm ⁻¹)	Ligand to Iron Ratio	Remarks
II	Red	528	8,800	2.9:1	(d) (f)
III	Colorless				
IV	Colorless				
V	Green	400 (a) 600	14,900 8,200	1.8:1	(c)
VI	Colorless				
VII	Colorless				
VIII	Blue	479 605	1,560 1,570	2.1:1	(c) (f)
IX	Colorless				
X	Orange-brown	470 620	19,400 5,700	2.2:1	(c)
XI	Orange-brown	442 522 644	22,000 13,700 5,900	2.2:1	(c)
XII	Green	558 633	6,000 6,400	2.0:1	(c)
XIII	Orange-brown	425 500 (a) 656 (a)	28,000 15,700 5,600	2.1:1	(c)
XIV	Green	608	4,200	(e)	(f) (g) (h)
XV	Green	610 (b)	800	2.8:1	(d) (f) (g)
XVI	Green	504 600 (a)	6,000 1,200	2.5:1	(d) (g)
XVII	Yellow-green	470 600 (b)	2,200 250	3.0:1	(d) (f) (g)
XVIII	Orange	498 600 (a)	9,400 3,600	3.2:1	(d) (f) (g)

(a) Shoulder. (b) Very broad band. (c) Little curvature in mole ratio plot indicating complex strongly formed. (d) Weak complex evidenced by appreciable curvature in mole ratio plot. (e) Complex too weak to identify reliably. (f) Color changes on standing one or more days. (g) Beer's law not followed unless large excess of ligand is added. (h) Insolubility of ligand required use of dimethylformamide as solvent.

EXPERIMENTAL

2-Quinolylmethyl 2-Pyridinyl Ketone (I).

To a suspension of sodium amide (prepared from 2.8 g. of sodium in 80 ml. of liquid ammonia), was slowly added 17.2 g. of quinaldine. After stirring for 0.5 hour, 7 g. of ammonium chloride were added and the ammonia allowed to evaporate overnight. The resulting solid was dissolved in water and neutralized with hydrochloric acid. The resulting precipitate, added to the residue from extraction of the aqueous filtrate with ether, was dried and crystallized from ethanol. The yield of pure product melting at 158° was 5.5 g. or 39.9%.

2-Quinolylmethyl Pyridinyl Ketone Oxime (II).

A mixture of the above ketone (1.25 g.), 1 g. of hydroxylamine hydrochloride, 1 g. of sodium hydroxide and 8 ml. of water was heated on the steam bath for 15 minutes. The precipitate obtained after cooling and acidification, was crystallized from methanol, yielding 0.5 g. of product melting at 204°.

Anal. Calcd. for C₁₆H₁₃N₃O: C, 72.99; H, 4.98; N, 15.96. Found: C, 72.73; H, 4.97; N, 15.74.

2-Quinolyl 2-pyridinyl Glyoxal 2-Oxime (III).

A solution of 1 g. of the above ketone in 16 ml. of 1-8 hydrochloric acid was added to 0.33 g. of sodium nitrite dissolved in 3.5 ml. of water. After one hour's standing, the mixture was made alkaline with ammonium hydroxide and the resulting precipitate crystallized from methanol. It melted at 175°.

Anal. Calcd. for C₁₆H₁₁N₃O₂: C, 69.31; H, 4.00; N, 15.15. Found: C, 69.28; H, 4.07; N, 15.03.

2-(1,10-Phenanthrolyl)methyl 2-Pyridinyl Ketone (IV).

To potassium ethoxide prepared from 0.05 g. atoms of potassium, was added 80 ml. of benzene, 0.05 mole of 2-methyl-1,10-phenanthroline and 0.025 mole of ethyl picolinate. The mixture was stirred at reflux for 6 hours. After cooling, water was added and the benzene layer was separated and dried over sodium sulfate. The aqueous layer was made neutral and extracted with ether. After removal of both solvents, the combined liquid was heated at 100° under an aspirator to remove unchanged reactants. The solid residue was then crystallized from benzene, yielding 4.3 g. (57.3% of pure product melting at 195°).

Table IV
Properties of Copper (I), Cobalt (II) and Nickel (II) Chelates

Ligand	Copper (I) Chelate			Cobalt (II) Chelate			Nickel (II) Chelate		
	Color	λ_{\max} (nm)	ϵ (l. mole ⁻¹ cm ⁻¹)	Color	λ_{\max} (nm)	ϵ (l. mole ⁻¹ cm ⁻¹)	Color	λ_{\max} (nm)	ϵ (l. mole ⁻¹ cm ⁻¹)
II	Gold	410	7,300 (c)	Yellow	450 (a)	2,000	Colorless		
III	Orange	483	4,300	Colorless			Colorless		
IV	(d)			(d)			(d)		
V	Gold	453	7,200	Yellow	475 (a)	3,400	Yellow	400 (a)	9,700
VI	(d)			(d)			(d)		
VII	Red	469	4,500 (b)	Colorless			Colorless		
VIII	Gold	438	3,800	Colorless			Colorless		
IX	Orange	475 (a)	4,500	Colorless			Colorless		
X	Red	512	12,300 (b)	Magenta	532	28,600	Orange	504	24,000
XI	Orange	497	21,600 (b)	Orange	492	27,500	Orange	505	42,000
XII	Gold	465	12,200	Gold	454	25,000	Yellow	464	42,500
XIII	Red	488	8,900 (b)	Red	514	24,300	Orange	496	39,000
XIV	Yellow	525 (a)	3,7000 (b)	(d)			(d)		
XV	Yellow	488 (a)	1,000	Green	575	7,000 (c)	(d)		
XVI	Gold	488 (a)	1,500	Green	584	5,000 (b) (c)	Orange	517	9,500
XVII	Yellow	425 (a)	3,000	Red	538	3,900	Yellow	463 (a)	4,300
XVIII	Orange	488 (a)	2,500 (c)	Brown	519	9,000 (b) (c)	Orange	488 (a)	12,600

(a) Not a maximum but a shoulder or side of ligand band just before absorption by free ligand is appreciable. (b) Color changes on standing one or more days. (c) Beer's law not followed unless large excess of ligand is present. (d) Same color (yellow) as that of free ligand.

Anal. Calcd. for $C_{19}H_{13}N_3O$: C, 76.24; H, 4.38; N, 14.04. Found: C, 75.69; H, 4.30; N, 13.93.

2-(1,10-Phenanthrolyl) 2-Pyridinyl Glyoxal 2-Oxime (V).

This compound was prepared from nitrous acid and dilute hydrochloric acid, as in the previous case. The pure product, crystallized from methyl cellosolve, melted at 238° .

Anal. Calcd. for $C_{19}H_{12}N_4O_2$: C, 69.51; H, 3.68; N, 17.06. Found: C, 69.21; H, 3.68; N, 16.77.

2-(1,10-Phenanthrolyl)methyl 2-Pyrazinyl Ketone (VI).

This compound was prepared like the corresponding 2-pyridinyl ketone using 0.03 mole each of potassium ethoxide and 2-methyl-1,10-phenanthroline, 0.15 mole of methyl pyrazinoate and 80 ml. of benzene. The yield of pure ketone, crystallized from benzene and melting at 217° , was 3.3%. No oximes could be made from this ketone.

Anal. Calcd. for $C_{18}H_{12}N_4O$: C, 71.99; H, 4.03; N, 18.66. Found: C, 72.22; H, 4.15; N, 18.70.

2-Acetyl-1,10-phenanthroline (VII).

A mixture of 0.025 mole each of freshly prepared sodium ethoxide, 2-carbethoxy-1,10-phenanthroline (7), ethyl acetate and 70 ml. of dry benzene was heated at reflux for 12 hours with stirring. The precipitated sodium enolate was then removed by filtration and the filtrate washed with water. To the washings was added enough water to make a total volume of 250 ml., to which the sodium enolate was added, and the mixture was acidified with 8 ml. of concentrated sulfuric acid. After heating 8 hours on the steam bath, the mixture was made alkaline with potassium hydroxide and the resulting precipitate dried and crystallized from methanol. The total yield of ketone melting at 154° was 1.9 g. (34.2%).

Anal. Calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.45; H, 4.49; N, 12.66.

Preparation of the Hydrazones of 2-Acetylquinoline and 2-Acetyl-1,10-phenanthroline (IX-XVIII).

A mixture of 0.004 mole each of ketone and substituted hydrazine and 1 ml. of acetic acid dissolved in 25 ml. of absolute ethanol was heated at reflux for 3 hours. After evaporation of the ethanol, the mixture was diluted with water and made alkaline with ammonium hydroxide. The resulting precipitate was dried and then crystallized from the solvent indicated in Tables I and II.

2-(2-Quinolyl)-1,10-phenanthroline (VIII).

A mixture of 0.015 mole each of 2-acetyl-1,10-phenanthroline and *o*-aminobenzaldehyde, and 1.9 ml. of 1*N* potassium hydroxide

in 25 ml. of ethanol was heated for 3 hours on a steam bath. Part of the ethanol was then removed by evaporation. The precipitate formed on addition of water was removed by filtration, dried and crystallized from methanol, yielding 1.0 g. (25.0%) of product melting at 194° .

Anal. Calcd. for $C_{21}H_{13}N_3$: C, 82.07; H, 4.26; N, 13.67. Found: C, 81.93; H, 4.31; N, 13.77.

Chelation Studies.

Procedures, reagents and standard solutions were similar to those described previously (10). Ascorbic acid was employed in place of hydroxylamine hydrochloride as the reductant in preparing complexes of iron(II), copper(I), and cobalt(II) to avoid possible conversion of the hydrazones to oximes. Solutions for spectrophotometric examination were adjusted to pH 7 by addition of 1*M* ammonium acetate. A Cary Model 14 spectrophotometer was used to record spectra. Results are compiled in Tables III and IV. Ligand to metal ratios of the iron(II) chelates, determined by the mole ratio method (11), are included in Table III.

Acknowledgement.

This publication was sponsored by the G. F. Smith Chemical Company, Columbus, Ohio.

REFERENCES AND NOTES

- (1) F. H. Case and A. A. Schilt, *J. Heterocyclic Chem.*, **14**, 1, (1977).
- (2) A. A. Schilt, N. Mohamed and F. H. Case, *Talanta*, **26**, 85 (1979).
- (3) N. Goldberg and R. Levine, *J. Am. Chem. Soc.*, **74**, 5217 (1952).
- (4) J. Behun and R. Levine, *ibid.*, **81**, 5157 (1959).
- (5) Von K. Madeja, *J. Prakt. Chem.*, **17**, 97 (1962).
- (6) K. Campbell, H. Helbing and J. Kerwin, *J. Am. Chem. Soc.*, **68**, 1840 (1946).
- (7) K. Claus and J. Rand, *Inorg. Chem.*, **8**, 59 (1969).
- (8) A. A. Schilt, "Analytical Applications of 1,10-Phenanthroline and Related Compounds", Pergamon, New York, N. Y., 1969, pp. 38-41.
- (9) A. A. Schilt, J. F. Wu and F. H. Case, *Talanta*, **22**, 915 (1975).
- (10) A. A. Schilt and K. R. Kluge, *ibid.*, **15**, 475 (1968).
- (11) A. S. Meyers and G. H. Ayres, *J. Am. Chem. Soc.*, **79**, 49 (1957).